Clinical Research Ethics Committee of the Cork Teaching Hospitals

APPLICATION FORM FOR A NEW STUDY

See Page 5 for list of documents required.

Please note that submission of an incomplete application pack will result in the application being returned to the study Chief Investigator. The application will not be reviewed.

Fully completed application packs will be accepted by CREC on the dates listed on page 3. Applications that are received after 4.30pm on the last day for submissions will not be reviewed at the next meeting. Replies will be sent to Study Chief Investigator only.

Send Applications to Lancaster Hall, 6 Little Hanover Street, Cork.
N.B. Do not send applications by AN POST REGISTERED post. The CREC office is not located on a registered post route and your application may be returned. Regular mail is recommended.

Chief Investigator Details

Name of Chief Investigator: Dr Peter Lee

Appointment: Consultant Anaesthetist

Hospital and Department: Cork University Hospital, Department of Anaesthesia

Address to which the response should be posted: Department of Anaesthesia, Cork University Hospital, Wilton, Cork

Contact Telephone Number: 021 4922135

Study Details

Study Number (if applicable):

Study Name: Perioperative Outcome Study in the Elderly (POSE): European, Large Scale, Multi-Centre, Prospective Observational Cohort Study

Study Sites (i.e. where will the study take place): Cork University Hospital & South Infirmary and Victoria University Hospital

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Co-Investigator Details

Names and Appointments of Study Co-Investigators:

Timothy Switzer, Specialist Registrar in Anaesthesia, Cork University Hospital
Shanmugasundaram Ramaswamy, Senior Lecturer in Anaesthesia, Cork University Hospital
Senbagam Rajamanickam, Registrar in Anaesthesia, Cork University Hospital
Please note that only the co-investigators listed above may perform the procedures indicated on this study. They may not amend study documentation.

Study Sponsor

If this study has received external funding complete the following: No

Name of Agency/Sponsor: N/A

Address of Agency/Sponsor: N/A

Does the Chief Investigator personally gain financially from this funding: No

Are there any additional cost implications for the hospital management beyond standard of care: No

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Study Insurance

A separate patient`s insurance will not be completed for this non-interventional observational trial.

Name of Insurer: N/A

Address: N/A

Complete the following for Patient Related Studies only. For non-interventional studies skip to "Details of the Purpose of the Study" Section

Special Considerations

Answer Yes or No to the following:

Is this study part of a multi-centre project: Yes

Does this study involve laboratory/clinical procedures NOT part of ordinary management: No

Does this study involve the clinical experimental use of radiation or radioisotopes: No

Does this study involve the use of biohazardous or infectious radioisotopes: No
If yes, please explain:

Are human subjects from the following special population(s) involved in this study:

Answer Yes or No to the following:

Infants (<1 Year): No

Children (1-17 years): No

Elderly (>59 years): Yes

Pregnant Women: No

Prisoners: No

Mentally Disabled: No

Mentally Retarded: No

None of these:

Study Description

Type of Study

Answer Yes or No to the following:

Behavioral-Social: No

Compassionate: No

Descriptive: Yes

Diagnostic: No

Educational: No

Epidemiologic: No

Preventive: No

Therapeutic: No

Other: Post operative outcome

Organ System(s):

Answer Yes or No to the following:

Not Applicable: Yes

Breast:

Cardiovascular:

Dermatologic:

Endocrine/Metabolic:

Gastrointestinal/Hepatic:

Haematologic:

Musculo-skeletal:

Neurologic:

Ophthalmologic:

Otolaryngologic:

Pulmonary:

Renal:

Reproductive:

Urinary tract:

Cells, blood, other body fluids or tissues only:

Other :

Type of Disorder:

Answer Yes or No to the following:

Not Applicable: Yes
Congenital:
Degenerative:
Infectious:
Immunologic:
Malignant:
Metabolic/Endocrine:
Normal Physiologic:
Psychiatric:
Traumatic
Other :

Type of Drug/Device:

Answer Yes or No to the following:

Not Applicable: Yes

Analgesics:

Anaesthetics:

Anti-asthma/allergy:

Anticoagulant:

Anti-infectives:

Anti-inflammatory/Anticonvulsants:

Biologicals/Vaccines:

Blood Components:

Cardiovascular/Antihypertensive:

Chemotherapeutic Agents:

Contraceptives

Contrast Media:

Dermatologics:

Diagnostics:

Hormones:

Immunosuppressives:

Vitamins:

Sedatives/Antidepressants/Tranquilizers:

Other:

Details of the Purpose of the Study: Include as much information as necessary to explain the study fully.

In Europe, it is estimated that the elderly population (≥80 years) will increase from 5.3% of the total population in 2015 to 9% in 2040. Of note, the 65-79 year and the ≥80 year old population will both continue to grow until 2040. The aforementioned demographic development suggests a dramatic growth in the number of elderly patients undergoing an increasing variety of surgical procedures, which entails that health care will need to adapt. Little is known about the in-hospital mortality rates in the elderly surgical population. The EUSOS study revealed an unexpectedly high in-hospital mortality rate of 4% in an unselected Pan-European non-cardiac surgery population. However, the EUSOS study did not specifically address the elderly population. POSE will go far beyond the EUSOS study as POSE will assess specifically the elderly surgical population, if in- or outpatient, elective or emergency surgery and it will also include cardiovascular surgery. Compared with younger surgical patients, the elderly are at greater risk of mortality and morbidity after elective and especially emergency surgery. The underlying mechanisms include age-related decline in physiological and cognitive reserve, and frequent comorbidities such as impaired hepatic and renal function, diabetes mellitus, dementia, delirium, coronary artery disease, heart failure, and patient poly-pharmacy. However data are mostly limited to specific higher risk populations, e.g. the elderly hip fracture patient. In these patients (≥65 years of age), the one-month mortality rate ranged from 8 to 10%. Most likely, the in-hospital mortality rate after outpatient and minor surgery will be much smaller than that following elective major and emergency surgery. Data are lacking in the overall elderly surgical population for: in-hospital mortality, the need for planned and unplanned admission to the intensive care unit, the use of non-standard monitoring tools, rate of non-extubation at the end of surgery and re-intubation rate, the surgical outcome, as well as length of hospital stay and the discharge destination. Furthermore, risk scores like the NSQIP and POSPOM need to be used in the elderly surgical population to improve risk communication and clinical decision making.

All these factors are of the utmost importance in planning both in and out of hospital health-care systems in Europe. All of the above underlines the urgent need to carry out this large scale, European multi-centre, and prospective observational cohort study.

POSE aims to be the first study to create a Europe-wide level of evidence on postoperative mortality and outcome in the elderly surgical population.

Primary Outcome: To determine the all-cause mortality up to 30-days after surgery.

Secondary Outcomes:

- To assess the new-onset (i.e. not pre-existing at time of surgery) of serious cardiac or pulmonary complications, acute stroke, or acute kidney injury up to 30-days after surgery.
- To assess postoperative in-hospital outcomes in compliance with the National Surgical Quality Improvement Program (NSQIP)
- To assess the proportion of not extubated patients at the end of surgery, or unplanned re-intubation within the hospital stay or maximum 30 days after surgery
- To assess the planned and unplanned admission rate to ICU within 30 days
- To assess the postoperative admission to a geriatric care unit
- To assess hospital- and ICU length of stay (LOS)
- To compare the postoperative in-hospital and 30-day outcome with preoperatively via NSQIP risk calculator and POSPOM predicted outcome
- To assess current practice of intraoperative monitoring for elderly surgical patients
- To identify differences in the geriatric perioperative management in health-care systems across Europe
- To assess the referring facility and discharge destination of the patients
- To determine the preoperative frailty of the patients
- To assess the perioperative functional status within 30 days after surgery

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Details of the Procedures to which humans will be subjected:

The participating patients will be subject to three encounters with the investigating team.

First encounter: Baseline visit preoperatively to ascertain patient demogaphics, baseline functional status, medical history, medication and recent laboratory results. A frailty assessment will also be performed, involving a cognitive assessment (Mini-Cog) and a timed ‘get up and go’ test. These are non-invasive verbal and observational tests that will completed on appropiate patients, and can be considered a standard of care.

Second encounter: Collection of intraoperative details including anaesthesia related details, surgery related details and ICU admission post operatively, both planned and unplanned.

Third encounter: Follow up on day 30 post operatively.
Medical record review to ascertain 30 day mortality, hospital and ICU length of stay and analysis of new onset of cardiac or pulmonary complications, acute stroke or acute kidney injury.

Brief telephone interview if patient was discharged, or brief face-to-face interview if the patient remains in hospital, on postoperative day 30 to assess mortality, serious cardiac/ pulmonary complications, stroke and acute kidney injury after hospital discharge. The patient`s functional status of independency will also be verbally assessed.

Potential benefits to subjects and/or society:

The POSE study will include a large sample of all surgical patients above the age of 80 years across the EU. This study population has been underrepresented in clinical trials to date. The results of this study may support health care systems to adapt to the patients´ needs (i.e. the need for critical care units for the elderly, more advanced monitoring devices, geriatricians in the surgical departments, or geriatric anaesthesia fellowship programs). Furthermore, the results may support future health facilities and budget planning.

Potential risks to subjects and precautions taken to minimise risk:

There is no risk for this non-interventional observational trial. Harms are not expected to any individual patient.

Alternative procedures, if any, available to subjects:

The patient may choose not to participate in the study.

Information on Patients/Participants/Audit

What is the total number of Patients/Participants to be studied? 75

How will the subjects be chosen (inclusion/exclusion criteria)?
Subjects, fulfilling the following inclusion criteria will be suitable for participation in the study:

- Age ≥80 years
- Written informed consent prior to study participation
- All consecutive patients undergoing surgical and non-surgical interventions (e.g. radiological, neuroradiological) with anaesthesia care within the selected inclusion period of four weeks
- Elective and emergency procedures

Subjects, fulfilling one or more of the following exclusion criteria will not be included in the study:

- People who are institutionalized by court or administrative order
- Patients with re-surgery within the 4 week period, who were already enrolled in this study

To ensure the generalizability of our data for elderly patients, we aim to include also legally incompetent patients with legally authorised representative/ health care proxy. Furthermore, we aim to include the emergency surgical population. We propose that it is important to include these patients to ensure that the study population is representative of the wider population of patients, and to avoid selection bias. Therefore, either legal representatives or relatives will receive detailed verbal and written information and will be asked to give verbal and written informed consent / assent, if the patient lacks the capacity to consent at this time-point.

How many charts will be reviewed if any?
75

Will participants receive payment/reward for participation in the study?
No

If so, provide details:

Chief Investigator Declaration

I certify that the protocol and method of obtaining informed consent as approved by the Ethics Committee will be followed during the period of this research project. Any changes

will be submitted for Ethics Committee review and approval prior to implementation. Any adverse reactions will be promptly reported to the Ethics Committee office. Only the approved Chief Investigator and Co-Investigators will carry out this research. All study records will be maintained and available for review by authorized persons from University College Cork and by the Department of Health & Children.

Signature Chief Investigator: _____

Print Name: _____

Date:

Clinical Research Ethics Committee Of The Cork Teaching Hospitals

AMENDMENT APPLICATION FORM

See Page 7 for list of documents required.

Please note that submission of an incomplete application pack will result in the application being returned to the study Chief Investigator. The application will not be reviewed.

The study title on this amendment application form must be exactly the same as the title on the original application.

Study Documents that have been changed due to this amendment must clearly show the changes (highlighted or tracked) and must contain a new version number and date. If the revised documents do not contain this information the application will be returned.

Chief Investigator Details

Name of Chief Investigator:

Hospital and Department:

Study Title:

The following changes are proposed for the study:

Answer Yes or No to the following:

Chief Investigator:

Co-investigator(s):

Dosage:

Treatment Procedures:

Drug/Device:

Study Population:

Number of Subjects:

Risks:

Answer Yes or No to the following:

Is a revised study protocol necessary as a result of this amendment?
If yes, please attach a revised protocol to this amendment.

Is a revised Participant Information Leaflet and Consent Form necessary as a result of this amendment?
If yes, please attach a revised consent form to this amendment.

Please list the specific changes from the previously approved protocol and provide sufficient rationale for each change to allow the committee to make a decision.

Chief Investigator Signature: _____ Date: _____

(This form must bear the original signature of the Chief Investigator)

Post Application to: Lancaster Hall, 6 Little Hanover Street, Cork

END OF TRIAL DECLARATION REPORT

Name of Chief Investigator:

Study Title:

Study Commencement Date:

Study Termination Date:

Brief description of the protocol:

Brief description of the results of the protocol:

Have any articles been published using the results of this study?
If yes, please submit a copy of the publication(s) to the Ethics Committee.

Total number of subjects recruited:

Total number of subjects who completed the project:

Any serious adverse reactions?
If yes, how many?

Were these reported to the Ethics Committee?

If not, please submit all serious adverse reactions to the Ethics Committee at this time.

Was this study terminated prematurely?
If yes give reasons why

I certify that as of the date below, subjects are no longer being studied or followed on the above protocol and therefore, this protocol should be officially terminated by the Ethics Committee.

Signature of Chief Investigator: _____ Date: _____

Post to: Lancaster Hall, 6 Little Hanover Street, Cork

Clinical Research Ethics Committee Of The Cork Teaching Hospitals

ANNUAL PROTOCOL RENEWAL SURVEY

PLEASE SEND TO CREC ANNUALLY FROM DATE OF ORIGINAL APPROVAL
Failure to submit an annual report will necessitate termination of the research.

Name of Chief Investigator:

Department/Hospital:

Address:

Study title:

Type of Study:

Organ System:

Disorder:

Drug or Device:

Special Populations:

Number of subjects recruited to date?

Answer Yes or No to the following:

Has the Study been terminated?

Has an End of Trial Declaration Form been submitted to CREC?

Has this study been changed in the past 12 months?

Have these changes been approved by the CREC?

Has any subjects on this study suffered an adverse reaction in the past 12 month?
If yes, have these adverse reactions been reported to the CREC?

Does this study involve the use of investigational drugs or devices?

If yes, name the Investigational drug or device used in this study

Will further subjects be enrolled into this study?
If not sure, indicate yes.

Was Informed Consent obtained?

Chief Investigator Signature: _____ Date: _____

Chairman Signature: _____ Date: _____

Clinical Research Ethics Committee Of The Cork Teaching Hospitals

Informed Consent

The Chief Investigator and Co-Investigators are responsible for:

- providing information on the research study to the study participants in a participant Information Leaflet
- obtaining informed consent on a Consent Form/Assent Form
- maintaining confidentiality

At the time consent is obtained, the subject must be competent to understand the procedure(s) and to freely give consent or be represented by a legally authorised representative. The Information Leaflet must fully inform participants of the nature of procedures to be undertaken and the risks, benefits and alternatives, if any, to the procedure(s).

It is understood that informed consent will always involve, or be based on, one or more conversations between the investigator, or a person designated by the Investigator, and the subject, or the subject's legally authorised representative. The written form which the subject signs serves as documentation that this dialogue has taken place and also as a record that the subject has agreed to participate in the research. The original signed consent form must be stored in the study Master File and a copy of the signed consent form must be given to the subject or subject's representative.

Special Populations

Regulations require that particular care be taken of subjects who are classified as special, vulnerable populations. These populations include:

- children (16 yrs and under)
- pregnant women
- prisoners
- students

When dealing with any of these populations, investigators are required to use a written consent form.

The Ethics Committee also requires particular care be taken of subjects who are classified in additional populations. These populations include:

- infants (under the age of one year)
- elderly (ages 60 and over)
- mentally disabled persons
- mentally retarded persons

No investigator shall recruit from a student group where he/she, or any of the co-investigators, has material influence over the assessment of academic performance of that student group.

Types of Consent

The manner in which consent is obtained from each subject will depend on the nature of the research protocol. There are two categories of informed consent:

- waiver of consent
- a signed written consent form

The following sections detail each type of informed consent and the conditions under which consent must be obtained.

1. Waiver of Informed Consent

The Ethics Committee will only consider a request for Waiver of Consent in the case of research, which does not come within the provisions of the Control of Clinical Trials Act 1987/1990.

The Ethics Committee may only waive the requirement for the Investigator to obtain a signed Consent Form for some or all subjects if either:

1. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research and the subject's wishes will govern. The Ethics Committee may nevertheless require the Investigator to provide subjects with a written statement regarding the research.

2. The research presents no more than minimal harm to subjects and involves no procedures for which written consent is normally required outside the research context.

Appropriate procedures for maintenance of confidentiality should be described in the protocol and in the Participant Information Leaflet. In cases where the consent requirements are waived, the Ethics Committee may require the investigator to provide subjects with a written statement regarding the research.

2. ***Written Consent***

In all other circumstances, a signed consent form is required. The written consent form may be read to the subject or the subject's legally authorised representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed. Also all written consents must have at least three sections which are headed as "Nature and Duration of Procedure", "Risks and Benefits", and "Alternatives". These paragraphs and sections are included in the sample consent form shown on Page 30. The written consent form must be typed in language easily understood by a person who has completed Primary School education.

Oral Consent

If a subject is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to subjects, is read and explained to the subject or the subject's legally acceptable representative, and after the subject or the subject's legally acceptable representative has orally consented to the subject's participation in the trial and, if capable of going so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and other written information was accurately explained to, and apparently understood by, the subject or the subject's legally acceptable representative, and that informed consent was freely given by the subject or the subject's legally acceptable representative.

Consent in Special Situations Relating to Category III Trials

1. Where a person is capable of comprehending the nature, significance and scope of the consent but is physically unable to give such consent, this consent clearly given in any other manner shall be sufficient where it is also given in the presence of two witnesses present at the same time, to a registered medical practitioner who is treating them for that illness and where the consent is expressed in writing and is attested by the signatures of both witnesses.

2. Where such a person is incapable of comprehending the nature and scope of the consent to be given. The person may participate in a trial only if a written and signed consent is given for such a participation by a legally acceptable representative independent of the person who applied to undertake or is conducting the trial who in the opinion of the Ethics Committee is competent to give a decision on such participation.

Elements of Informed Consent

Informed consent, whether written or oral, must include the following elements.

A statement that the protocol involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures, drugs and devices which are experimental.

1. Description of any reasonably foreseeable risks or discomforts to the subject.
2. Description of any benefits to the subject or to others that may reasonably be expected from the research, including payment or free treatment.
3. A disclosure of appropriate alternative procedures or courses of treatment, if applicable, that might be advantageous to the subject.
4. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained.
5. For research involving more than minimal risk, a statement that in the vent of physical injury, free emergency care only will be provided if necessary.
6. A statement as to whom to contact (a single individual) for answers to pertinent questions involving the research and research subject's rights, and whom to contact in the event of a research-related injury to the subject.
7. A statement similar to "participation is voluntary" or "you may choose not to participate". And a statement that refusal to participate, or discontinuing participation at any time, will involve no penalty, loss of benefits or denial of treatment or services. This statement should be included in the alternatives section of the consent if there is no alternative procedure but is always part of the "agreement to consent" section.

When appropriate, one or more of the following additional elements of information should be included in the informed consent:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or foetus, if the subject is to become pregnant) that is currently unforeseeable.
2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequence of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
5. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
6. The approximate number of subjects involved in the study.

The Consent Form *must* also include the following:

1. A provision for subjects to be given a copy of the consent form, if the consent is written.
2. If blood is to be withdrawn, the standard blood withdrawal information including: amount of blood to be withdrawn (in teaspoons or tablespoons); number of times; period of time covered; potential hazards, such as "a bruise at the site of vein puncture, inflammation of the vein and possible infection", and information that "care will be taken to avoid these complications".

The Consent Form *may not* include:

The consent may not include any exculpatory language through which the subject is made to waive or appear to waive any legal rights or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Pregnancy Clause

If women of childbearing age will be used as subjects and pregnancy is an exclusion criterion, state in the protocol and consent form that a pregnancy test will be given prior to subject's entry into the study. In addition, state that subjects must abstain from sexual intercourse or use appropriate contraception after the pregnancy test until study initiation and throughout the duration of the study.

It should also be stated in the consent form that if the subject becomes pregnant during the course of the study, the subject must notify the chief investigator as soon as possible.

Consent and Assent from Children

Individuals under the age of 16 (unless the individual is a legally emancipated minor) cannot legally consent to being involved in research protocols. The permission of both parents is generally required. One parent may consent when there is no more than minimal risk or if there is more than minimal risk but presents the prospect of direct benefit to the individual subject. Both parents consent is required for research involving greater than minimal risk unless one parent is deceased, unknown, incompetent or not reasonably available or when only one parent has legal responsibility for the care and custody of the child.

Additionally, the assent of the participating child must also be obtained from all children with a capacity to understand the research to be done. This assent is simply an indication of agreement by the child to his or her involvement in the research protocol, which must be explained to him or her in language the child can understand. This personal assent must be documented on the written consent form and in the child's medical record.

There are only two circumstances in which children with the capacity to assent may be enrolled in a research protocol without their assent. The first situation is when the Ethics Committee (<u>not</u> the investigator) determines that the ability to understand some or all of the children involved is so limited that they cannot be reasonably consulted (because of age, maturity, or mental state). The children's assent may also be waived when it is evident that the intervention or procedure involved in the research shows a prospect of direct benefit that is important to the health or well-being of the specific child (subjects) and is available only in this context.

Subjects Unavailable to give Consent

In the case of emergency studies involving subjects so ill that they are unable to give informed consent, the Ethics Committee will deal with the consent process on a case-by-case basis. In such instances, any research undertaken must be related to the emergency treatment. Similarly, when substitutes or surrogates are to consent for research subjects, the consent process must be detailed in the protocol and the justification for substituted consent freely explained. Generally, only legally authorised representatives may substitute their consent for the consent of a research subject.

Consent Form Records

All original signed consent forms for each subject must be kept on file in the subject's medical record in the hospital medical records or the study Master File. Medical records should be initiated for all subjects who are not already patients at the hospital including normal volunteers participating in research studies. A copy of the signed consent form must be given to the subject, and further copy must be kept by the Chief Investigator.

CONSENT BY SUBJECT FOR PARTICIPATION IN RESEARCH STUDY

Study Number (if applicable): **Patient Name:**_____

Study Title (study title must be exactly the same on all study documentation):

Name of Chief Investigator:

Contact Number for Chief Investigator:

You are being asked to participate in a research study. The doctors at _____study the nature of disease and attempt to develop improved methods of diagnosis and treatment. In order to decide whether or not you want to be a part of this research study, you should understand enough about its risks and benefits to make an informed judgment. This process is known as informed consent. This consent form gives detailed information about the research study. The Chief Investigator will also discuss the study with you in detail. When you are sure you understand the study and what will be expected of you, you will be asked to sign this form if you wish to participate.

NATURE AND DURATION OF PROCEDURE(S):

This section should begin with a summary paragraph describing the purpose of the study. Address the section to the subject (e.g. you will be...). It should be written in non-technical, easy-to-understand, primary school language. The section should include details of who will be conducting the study/procedure(s)/interviews, where it will take place, for how long and how many study visits. **Any tests or procedures the subject will undergo should be explained in detail.**

POTENTIAL RISKS AND BENEFITS:

Risks (both psychological and physical) to all tests and procedures, must be reasonably detailed. This section should describe potential general benefits of the research (ex. benefits to society), as well as benefits to the individual. Again, address the subject (you, your...).

POSSIBLE ALTERNATIVES:

This section should describe all possible alternatives to this study whether it be other treatments, or no treatment at all. If no treatment is the option, the section should read, "you may choose not to participate, or participation is voluntary". **"None" and "not applicable" are not appropriate alternatives.**

AGREEMENT TO CONSENT

The research project and the treatment procedures associated with it have been fully explained to me. All experimental procedures have been identified and no guarantee has been given about the possible results. I have had the opportunity to ask questions concerning all aspects of the project and any procedures involved. I am aware that participation is voluntary and that I may withdraw my consent at any time. I am aware that my decision not to participate or to withdraw will not restrict my access to health care services normally available to me. Confidentiality of records concerning my involvement in this project will be maintained in an appropriate manner. When required by law, the records of this research may be reviewed by government agencies and sponsors of the research.

I understand that the sponsors and investigators have such insurance as is required by law in the event of injury resulting from this research.

I, the undersigned, hereby consent to participate as a subject in the above described project conducted at _____. I have received a copy of this consent form for my records. I understand that if I have any questions concerning this research, I can contact the Chief Investigator listed above. I understand that the study has been approved by the Cork Research Ethics Committee of the Cork Teaching Hospitals (CREC) and if I have further queries concerning my rights in connection with the research, I can contact CREC at Lancaster Hall, 6 Little Hanover Street, Cork, 021 4901901.

Answer yes or no or insert tick boxes

I have read and understand the study:

I agree to participate in this research:

If the study involves interviews/focus groups that will be audio-recorded the following sentence should be added:

I agree to allow my interview/focus group to be audio-recorded:

I grant permission for the data collected to be used in this research only:

I understand that my anonymised data will be stored at _____ for _____ years:

Chief Investigator Signature: _____

Signature of Study Participant: _____

Witness Signature (if applicable): _____

Legal Representative Signature (if applicable) _____

Date: _____

Consent Form Version Number: _____ Date: _____

Genetic Research

Human Tissue and Biological Samples for Use in Genomic Research, Operational and Ethical Guidelines
Following on from rapid developments in knowledge of the human genome sequence, large numbers of well documented human DNA samples are essential for the research needed to translate this knowledge into real benefits for public health and health care. In view of widespread concern about confidentiality and ethical issues related to genetic research the Clinical Research Ethics Committee has established the general principles that could also govern the use of collections of human DNA samples.

Special Issues Related to Collection of Human Material
Collections of human material are very important in medical research. There are, however, a number of special issues in relation to samples of human tissue.

Samples can be stored for a long time and may be of considerable value for research that was not, and could not have been, envisaged at the time the material was obtained.
Using materials for studies not planned at the time that they were obtained raises difficult ethical issues in relation to consent.
It is often not possible to, and usually not practicable, to go back to the donor for new consent.
Information obtained from research using biological samples can have implications for the individual donor and their relatives.

Genetic research on stored samples can give rise to particular concerns in relation to the implications for insurance, privacy, and the potential impact on the relatives of the donor of the sample.

Ownership
For research, the important consideration is not legal ownership, *per se*, but who has the right to control the use of samples or their transfer to a third party. Therefore these guidelines focus on the custodianship of samples and the control of their use.

We recommend that tissue samples donated for research be treated as gifts. Gifts may be conditional (that is, a donor may specify what the recipient can do with the gift). It is therefore important that the donor understands and agrees to the proposed uses of donated material. When consent is obtained the donor needs to understand that he/she is making a donation of a sample for use in research, and who will be responsible for the custodianship of the sample.

There are circumstances, for instance in the case of tissue removed in the course of surgical treatment or excess material left over after diagnostic testing, where patients might be considered legally to have "abandoned" their tissue. However, the Clinical Research Ethics Committee recommends that consent should be obtained at the time the tissue is taken for use for research of tissue surplus to clinical requirement. The material can then be treated as a donation from the patient to the institution or the department responsible for the treatment or diagnosis. Some hospitals have modified their routine admission and surgical consent forms to include consent for use of surplus tissue for research and teaching, and we strongly recommend that this practice be more widely adopted. However, there must be explicit separation of the consent to the treatment or diagnostic test from the consent to the use of surplus tissue for research.

While reasonable expenses (e.g. travel expenses) may be reimbursed, research participants should never be offered any financial or material inducement to donate biological samples for research.

Custodianship and Access
If samples are to be treated as gifts, there must be a recipient, to whom formal responsibility for the custodianship of a donated sample is transferred. While the chief investigator should have day-to-day responsibility for the management of a sample collection, the Clinical Research Ethics Committee considers

that it is more appropriate for formal responsibility for custodianship of sample collections to rest with the institution rather than with the individual researchers.

Commercial Exploitation
It is essential that research participants be made aware that their sample or products derived from it may be used by the commercial sector, and that they will not be entitled to a share of any profits that might ensue.

Confidentiality and Anonymisation
People who donate samples for research must be told what information about their medical history or other personal details will be used in the research, who it might be shared with, what safeguards are in place to preserve confidentiality, and give explicit consent to these arrangements. Personal data should be stored, processed and analysed in a form that does not allow individuals to be identified, unless there is a strong ethical or scientific justification for not doing so. Identifiable data should only be accessible to staff who have a formal duty of confidence to the participant.

Wherever possible samples and associated data should be anonymised or coded. In addition, identifiable data should not be transferred to a country outside the European Union unless it has an equivalent data protection regime.

Consent
When obtaining consent to take a tissue sample for research, it is important to allow for the fact that the sample might subsequently be used for new experiments that cannot be foreseen. Therefore, unless a sample is to be used only for a single project consent must be obtained for storage and for future use or research. **A two-part consent process is recommended**, the donor being first asked to consent to the specific experiments that are already planned, and then give a broader consent for storage and future use for certain types of research. Where a two-part consent process is used they must always be given the option of specifying that their sample may only be used for the research project already planned.

Feedback of Information
Researchers must decide at the outset what their strategy will be with regard to feeding back information and whether any linkage of research results to individuals will be possible. This must be set out in their submission to the Ethics Committee, and the policy adopted must be explained to research participants before they consent to take part in the research. Research results obtained on anonymised samples cannot have any impact on the interest of an individual donor and cannot be fed back. On the other hand, irreversibly breaking the link between a sample and an individual can significantly reduce its value for research, for instance by making it impossible to add follow-on data or to audit research results. There are various possible strategies for anonymisation; samples can be irreversibly anonymised from the outset, or they can be anonymised after the initial study is done, either before being used for any secondary use or before use in specific studies only. Where a result that can be linked to an individual has immediate clinical relevance, for example, if it reveals a serious condition for which treatment is required, the clinician involved has a clear duty of care to inform the research participant, either directly or via the clinician responsible for his or her care. It is good clinical practice to offer research participants the opportunity to be kept informed about the general results of research projects done using samples they have donated, though this may not be appropriate in all circumstances.

What research can be done using old samples?
Generally, established collections can be used for research when samples have been coded or anonymised, and there is no potential harm to the donors of the material, individually or as a group.

When is it necessary to consult the Ethics Committee
The Clinical Research Ethics Committee considers that Ethics Committee approval should be obtained for all new research not specifically mentioned when consent was originally obtained in previous Ethics Committee submissions. This is an important means of safeguarding the interests of the donors.

SAMPLE CONSENT FOR GENETIC RESEARCH

Study Title: _____

Study Chief Investigator: _____

Contact Details: _____

Participant Please Initial Boxes

1. I have read the attached information leaflet on the above project dated ……. and have been supplied with a copy. The information has been fully explained to me.	
2. I agree to give a sample of DNA for the above research. I agree that my sample and the information gathered from me can be stored in computer or manual format and looked after by the ……..	
3. I give permission for my medical records to be reviewed and information to be taken from them to be analysed in confidence by ……	
4. I understand that all medical information pertaining to me, including my samples, will be protected by the principles of confidentiality and both National and EU Data Protection Legislation.	
5. I agree to the storage of my samples at …….. for ……..years for use later in genetic research pertaining to …….	

Participant Signature: _____ **Date:** _____